

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Shinji OKANO et al.	Confirmation No.:	5137
Serial No.:	10/578,085	Art Unit:	1645
371(c) Date:	May 3, 2006	Examiner:	Not Yet Assigned
		Customer No.:	21559
Title:	METHOD FOR PRODUCING GENE TRANSFERRED DENDRITIC CELLS (as amended)		

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST TO CORRECT FILING RECEIPT

Applicant requests that the enclosed filing receipt be corrected as follows.

In the **Power of Attorney** section, please change "39905" to --21559--.

In the **Title** section, please change "Denritic" to --Dendritic--.

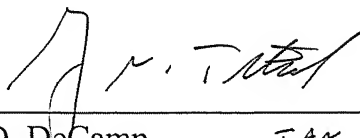
Enclosed, in support of the above corrections, are copies of the incorrect filing receipt, the Reply to Notification of Missing Requirements and Combined Declaration and Power of Attorney as filed on April 30, 2007, and the Application Data Sheet and Preliminary Amendment as filed with the application on May 3, 2006.

If there are any charges or any credits, please apply them to Deposit Account No.

03-2095.

Respectfully submitted,

Date: 21 August 2007



James D. DeCamp
Reg. No. 43,580

JAN M. TITZER, Ph.D.
Reg. No. 52,290

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
Facsimile: 617-428-7045



UNITED STATES PATENT AND TRADEMARK OFFICE

De-Docketed

UNITED STATES DEPARTMENT OF COMMERCE
 United States Patent and Trademark Office
 Address: COMMISSIONER FOR PATENTS
 P.O. Box 1450
 Alexandria, Virginia 22313-1450
 www.uspto.gov

APPL NO.	FILING OR 371(c) DATE	ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO	TOT CLMS	IND CLMS
10/578,085	05/03/2006	1645	1440	50026/058001	14	2

CONFIRMATION NO. 5137

21559
 CLARK & ELBING LLP
 101 FEDERAL STREET
 BOSTON, MA 02110

FILING RECEIPT



OC000000025334218

Date Mailed: 08/13/2007

Receipt is acknowledged of this nonprovisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Filing Receipt Corrections. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).**

Applicant(s)

Shinji Okano, Fukuoka, JAPAN;
 Yoshikazu Yonemitsu, Fukuoka, JAPAN;
 Katsuo Sueishi, Fukuoka, JAPAN;
 Satoko Shibata, Fukuoka, JAPAN;
 Mamoru Hasegawa, Ibaraki, JAPAN;

Power of Attorney: The patent practitioners associated with Customer Number ~~39905~~ 21559.

Domestic Priority data as claimed by applicant

This application is a 371 of PCT/JP04/16089 10/29/2004

Foreign Applications

JAPAN 2004-187028 06/24/2004
 JAPAN 2003-374808 11/04/2003

If Required, Foreign Filing License Granted: 08/11/2007

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US10/578,085**

Projected Publication Date: 11/22/2007

Non-Publication Request: No

Early Publication Request: No

Title

Dendritic
Method for Producing Gene Transferred Dendritic Cells

Preliminary Class

435

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at <http://www.uspto.gov/web/offices/pac/doc/general/index.html>.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, <http://www.stopfakes.gov>. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4158).

LICENSE FOR FOREIGN FILING UNDER Title 35, United States Code, Section 184 Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The

date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

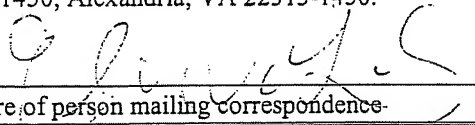
The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign Assets Control, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

COPY

PATENT
ATTORNEY DOCKET NO. 50026/058001

Certificate of Mailing	
Date of Deposit: <u>April 30, 2007</u>	Label Number: <u>EV919880884US</u>
I hereby certify under 37 C.F.R. § 1.10 that this correspondence is being deposited with the United States Postal Service as "Express Mail Post Office to Addressee" with sufficient postage on the date indicated above and is addressed to Mail Stop PCT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.	
<u>Elvis De La Cruz</u> Printed name of person mailing correspondence	 Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Shinji Okano et al.	Confirmation No.:	5137
Serial No.:	10/578,085	Art Unit:	Not yet assigned
Filed:	May 3, 2006	Examiner:	Not yet assigned
Customer No.:	21559		
Title:	METHOD FOR PRODUCING GENE TRANSFERRED DENDRITIC CELLS		

Mail Stop PCT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-145

REPLY TO NOTIFICATION OF MISSING REQUIREMENTS

In reply to the Notification of Missing Requirements that was mailed in connection with the above-captioned application on March 12, 2007, a copy of which is enclosed¹, Applicants, as a large entity, submit the following:

A Combined Declaration and Power of Attorney in compliance with 37 C.F.R. § 1.497(a) and (b), identifying the application by the international application number and international filing date.

¹ A copy of the Cover Letter for Resending Correspondence mailed on April 5, 2007 is also enclosed. The Notification of Missing Requirements was originally mailed to the incorrect address.

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A surcharge under 37 C.F.R. § 1.492(h) of \$130.00, because the declaration is being submitted after 30 months from the priority date.

Applicants note that the Notification of Missing Requirements also states that a translation of the application into English and the processing fee for this translation are required. Applicants, for the reasons set forth below, submit that this requirement is in error.

The application, as filed on May 3, 2006, included an English language translation of international application number PCT/JP2004/016089. Enclosed, as Exhibit 1, is a copy of the return postcard included with the May 3, 2006 filing and listing the English language translation. The return postcard bears the U.S.P.T.O. stamp indicating receipt of the items listed on the postcard by the U.S.P.T.O. on May 3, 2006. In accordance with the M.P.E.P. § 503, the postcard clearly identifies and itemizes the items for which a receipt was requested. As such, Applicants submit that this postcard receipt provides *prima facie* evidence that an English language translation was filed with the U.S.P.T.O. on May 3, 2006.

Moreover, Applicants submit, as Exhibit 2, a printout image of the Image File Wrapper (IFW) summary for the present application from the U.S. Patent Application Information (PAIR) website. The IFW includes the items listed on the return postcard and indicates that these items were received by the U.S.P.T.O. on May 3, 2006. Enclosed, as Exhibit 3, is a copy of the English language translation as printed from the IFW which has been date stamped May 3, 2006 by the U.S.P.T.O. and sets forth the serial

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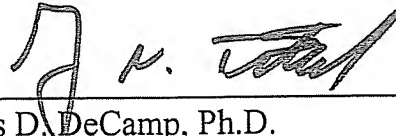
number for the present application.

For all the above reasons, Applicants submit that the English language translation of the present application was filed with the application on May 3, 2006. Also, as the May 3, 2006 filing date of the English language translation was within 30 months of the priority date, Applicants submit that no additional processing fee for the filing of the translation is due.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 30 April 2007



James D. DeCamp, Ph.D.
Reg. No. 43,580

JAN M. FITTEL, Ph.D.
Reg. No. 52,290

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
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UNITED STATES DEPARTMENT OF COMMERCE
 United States Patent and Trademark Office
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U.S. APPLICATION NUMBER NO.	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
10/578,085	Shinji Okano	50026/058001

INTERNATIONAL APPLICATION NO.

PCT/JP04/16089

I.A. FILING DATE

10/29/2004

PRIORITY DATE

11/04/2003

39905
 ROETZEL AND ANDRESS
 222 SOUTH MAIN STREET
 AKRON, OH 44308

CONFIRMATION NO. 5137

371 FORMALITIES LETTER



OC000000022816390

Date Mailed: 03/12/2007

NOTIFICATION OF MISSING REQUIREMENTS UNDER 35 U.S.C. 371 IN THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US)

The following items have been submitted by the applicant or the IB to the United States Patent and Trademark Office as a Designated / Elected Office (37 CFR 1.495).

- Copy of the International Application filed on 05/03/2006
- Copy of the International Search Report filed on 05/03/2006
- Copy of IPE Report filed on 05/03/2006
- Preliminary Amendments filed on 05/03/2006
- Biochemical Sequence Diskette filed on 05/03/2006
- Oath or Declaration filed on 05/03/2006
- Biochemical Sequence Listing filed on 05/03/2006
- U.S. Basic National Fees filed on 05/03/2006
- Priority Documents filed on 05/03/2006

The applicant needs to satisfy supplemental fees problems indicated below.

The following items **MUST** be furnished within the period set forth below in order to complete the requirements for acceptance under 35 U.S.C. 371:

- Translation of the application into English. Note a processing fee will be required if submitted later than 30 months from the priority date.
- Processing fee of \$130 for providing the translation of the application and/or the Annexes later than 30 months from the priority date (37 CFR 1.492(i)).
- Oath or declaration of the inventors, in compliance with 37 CFR 1.497(a) and (b), identifying the application by the International application number and international filing date. The current oath or declaration does not comply with 37 CFR 1.497(a) and (b) in that it:
 - is not executed in accordance with either 37 CFR 1.66 or 37 CFR 1.68.

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- To avoid abandonment, a surcharge (for late submission of filing fee, search fee, examination fee or oath or declaration) as set forth in 37 CFR 1.492(h) of \$130 for a non-small entity, must be submitted with the missing items identified in this letter.

SUMMARY OF FEES DUE:

Total additional fees required for this application is **\$-150** for a Large Entity:

- **\$130** Surcharge.
- **\$130** for English translation surcharge required.

(A previous payment of **\$410** will be applied to the additional fees indicated above.)

ALL OF THE ITEMS SET FORTH ABOVE MUST BE SUBMITTED WITHIN TWO (2) MONTHS FROM THE DATE OF THIS NOTICE OR BY 32 MONTHS FROM THE PRIORITY DATE FOR THE APPLICATION, WHICHEVER IS LATER. FAILURE TO PROPERLY RESPOND WILL RESULT IN ABANDONMENT.

The time period set above may be extended by filing a petition and fee for extension of time under the provisions of 37 CFR 1.136(a).

Applicant is reminded that any communications to the United States Patent and Trademark Office must be mailed to the address given in the heading and include the U.S. application no. shown above (37 CFR 1.5)

Registered users of EFS-Web may alternatively submit their reply to this notice via EFS-Web.
<https://sportal.uspto.gov/authenticate/AuthenticateUserLocalEPF.html>

For more information about EFS-Web please call the USPTO Electronic Business Center at 1-866-217-9197 or visit our website at <http://www.uspto.gov/ebc>.

If you are not using EFS-Web to submit your reply, you must include a copy of this notice.

PATRICIA A BOOKER

Telephone: (703) 308-9140 EXT 204

PART 1 - ATTORNEY/APPLICANT COPY

U.S. APPLICATION NUMBER NO.	INTERNATIONAL APPLICATION NO.	ATTY. DOCKET NO.
10/578,085	PCT/JP04/16089	50026/058001

COPY

PATENT
ATTORNEY DOCKET NO. 50026/058001

COMBINED DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name.

I believe I am the original, first, and sole inventor (if only one name is listed below) or an original, first, and joint inventor (if plural names are listed below) of the subject matter that is claimed and for which a patent is sought on the invention entitled METHOD FOR PRODUCING GENE TRANSFERRED DENDRITIC CELLS, the specification of which was filed on May 3, 2006 as Application Serial No. 10/578,085 and is that of PCT/JP2004/16089, filed October 29, 2004.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims.

I acknowledge the duty to disclose all information I know to be material to patentability in accordance with 37 C.F.R. § 1.56.

FOREIGN PRIORITY RIGHTS: I hereby claim foreign priority benefits under 35 U.S.C. § 119(a)-(d) or (f), or § 365(b) of any foreign application(s) for patent, inventor's or plant breeder's rights certificate(s), or § 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below, and have also identified below any foreign application for patent, inventor's or plant breeder's rights certificate(s), or any PCT international application having a filing date before that of the application on which priority is claimed.

Country	Serial Number	Filing Date	Priority Claimed
JP	2003-374808	November 4, 2003	Yes
JP	2004-187028	June 24, 2004	Yes

PROVISIONAL PRIORITY RIGHTS: I hereby claim priority benefits under 35 U.S.C. § 119(e) of any United States provisional patent application(s) listed below filed by an inventor or inventors on the same subject matter as the present application and having a filing date before that of the application(s) of which priority is claimed:

Serial Number	Filing Date	Status

NON-PROVISIONAL PRIORITY RIGHTS: I hereby claim the benefit under 35 U.S.C. § 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of 35 U.S.C. § 112, I acknowledge the duty to disclose all information I know to be material to patentability as defined in 37 C.F.R. § 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

Serial Number	Filing Date	Status


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I hereby appoint the attorneys and/or agents associated with customer number **21559** to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith.

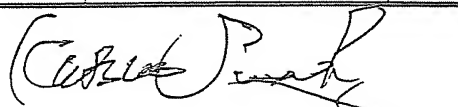
Address all correspondence relating to this application to the address associated with customer number **21559**.

Address all telephone calls to: James D. DeCamp at 617-428-0200.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001, and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Full Name (First, Middle, Last)	Residence Address (City, State, Country)	Post Office Address (Street, City, State, Country)	Country of Citizenship
Shinji OKANO	FUKUOKA, Japan	15-3-301, Yoshizuka 4-chome, Hakata-ku, Fukuoka-shi, FUKUOKA 812-0041 JAPAN	Japan
Signature: 			Date: July 17, 2006

Full Name (First, Middle, Last)	Residence Address (City, State, Country)	Post Office Address (Street, City, State, Country)	Country of Citizenship
Yoshikazu YONEMITSU	FUKUOKA, Japan	5-31-3, Najima, Higashi-ku, Fukuoka-shi, FUKUOKA 813-0043 JAPAN	Japan
Signature: 			Date: 7/24/2006

Full Name (First, Middle, Last)	Residence Address (City, State, Country)	Post Office Address (Street, City, State, Country)	Country of Citizenship
Katsuo SUEISHI	FUKUOKA, Japan	1-29-22, Oike, Minami-ku, Fukuoka-shi, FUKUOKA 815-0073 JAPAN	Japan
Signature: 			Date: Jul. 24, '06

COPY

Full Name (First, Middle, Last)	Residence Address (City, State, Country)	Post Office Address (Street, City, State, Country)	Country of Citizenship
Satoko SHIBATA	FUKUOKA, Japan	2-14-15-701, Hakomatsu, Higashi-ku, Fukuoka-shi, FUKUOKA 812-0061 JAPAN	Japan
Signature: <i>Satoko Shibata</i>			Date: <i>7/24/2006</i>

Full Name (First, Middle, Last)	Residence Address (City, State, Country)	Post Office Address (Street, City, State, Country)	Country of Citizenship
Mamoru HASEGAWA	IBARAKI, Japan	c/o DNAMEC Research Inc., 25-11, Kannondai 1-chome, Tsukuba-shi, IBARAKI 305-0856 JAPAN	Japan
Signature: <i>長瀬 護</i>			Date: <i>7/27/2006</i>

COPY

Application Data Sheet

Application Information

Application number::

Filing Date:: 05/03/06

Application Type:: Regular

Subject Matter:: Utility

Suggested Classification::

Suggested Group Art Unit::

CD-ROM or CD-R?:: None

Number of CD disks::

Number of copies of CDs::

Sequence submission?::

Computer Readable Form (CRF)?::

Number of copies of CRF::

Title:: METHOD FOR PRODUCING GENE
TRANSFERRED DENDRITIC CELLS (AS
AMENDED)

Attorney Docket Number:: 50026/058001

Request of Early Publication?:: No

Request of Non-Publication?:: No

Small Entity?:: No

Petition Included?:: No

Applicant Information

Applicant Authority Type:: Inventor

Primary Citizenship Country:: Japan

Copy

Status:: Full Capacity
Given Name:: Shinji
Family Name:: Okano
City of Residence::
State or Province of mailing address:: Fukuoka
Country of Residence:: Japan
Street of mailing address:: 15-3-301, Yoshizuka 4-chome, Hakata-ku,
City of mailing address:: Fukuoka-shi
State or Province of mailing address:: Fukuoka
Country of mailing address:: Japan
Postal or Zip Code of mailing address:: 812-0041

Applicant Authority Type:: Inventor
Primary Citizenship Country:: Japan
Status:: Full Capacity
Given Name:: Yoshikazu
Family Name:: Yonemitsu
City of Residence::
State or Province of mailing address:: Fukuoka
Country of Residence:: Japan
Street of mailing address:: 5-31-3, Najima, Higashi-ku
City of mailing address:: Fukuoka-shi
State or Province of mailing address:: Fukuoka
Country of mailing address:: Japan
Postal or Zip Code of mailing address:: 813-0043



Applicant Authority Type:: Inventor
Primary Citizenship Country:: Japan
Status:: Full Capacity
Given Name:: Katsuo
Family Name:: Sueishi
City of Residence::
State or Province of mailing address:: Fukuoka
Country of Residence:: Japan
Street of mailing address:: 1-29-22, Oike, Minami-ku
City of mailing address:: Fukuoka-shi
State or Province of mailing address:: Fukuoka
Country of mailing address:: Japan
Postal or Zip Code of mailing address:: 815-0073

Applicant Authority Type:: Inventor
Primary Citizenship Country:: Japan
Status:: Full Capacity
Given Name:: Satoko
Family Name:: Shibata
City of Residence::
State or Province of mailing address:: Fukuoka
Country of Residence:: Japan
Street of mailing address:: 2-14-15-701, Hakomatsu, Higashi-ku
City of mailing address:: Fukuoka-shi

COPY

State or Province of mailing address:: Fukuoka

Country of mailing address:: Japan

Postal or Zip Code of mailing address:: 812-0061

Applicant Authority Type:: Inventor

Primary Citizenship Country:: Japan

Status:: Full Capacity

Given Name:: Mamoru

Family Name:: Hasegawa

City of Residence::

State or Province of mailing address:: Ibaraki

Country of Residence:: Japan

Street of mailing address:: c/o DNAMEC Research, Inc., 25-11, Kannondai 1-chome

City of mailing address:: Tsukuba-shi

State or Province of mailing address:: Ibaraki

Country of mailing address:: Japan

Postal or Zip Code of mailing address:: 305-0856

Correspondence Information

Correspondence Customer Number:: 21559

Representative Information

Representative Customer Number:: 21559

Domestic Priority Information

Application:: Continuity Type:: Parent Application:: Parent Filing Date::

COPY

This Application National stage of PCT/JP2004/016089 10/29/04

Foreign Priority Information

Country::	Application Number::	Filing Date::	Priority Claimed::
JP	2004-187028	06/24/04	YES
JP	2003-374808	11/04/03	YES

Assignee Information

Assignee name::

Street of mailing address::

City of mailing address::

State of Province of mailing address::

Country of mailing address::

Postal or Zip Code of mailing address::

COPY

PATENT
ATTORNEY DOCKET NO. 50026/058001

Certificate of Mailing

Date of Deposit: May 3, 2006

Label Number: EV919876071US

I hereby certify under 37 C.F.R. § 1.10 that this correspondence is being deposited with the United States Postal Service as "Express Mail Post Office to Addressee" with sufficient postage on the date indicated above and is addressed to Mail Stop PCT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

ELVIS DELACRUZ

Printed name of person mailing correspondence


Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Shinji Okano et al. Art Unit: Not yet assigned

Serial No.: Not yet assigned Examiner: Not yet assigned

Filed: May 2, 2006 Customer No.: 21559

Title: METHOD FOR PRODUCING GENE TRANSFERRED
DENDRITIC CELLS (as amended)

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PRELIMINARY AMENDMENT

Prior to examination of the above-captioned application, kindly amend the application as follows. Please note that all page and line number references in the present amendment refer to the concurrently filed English language translation of International Application No. PCT/JP2004/016089, of which the above-captioned application is the U.S. National Stage.

COPY

AMENDMENTS TO THE SPECIFICATION

Kindly amend the title of the application as follows.

METHOD OF CONSTRUCTING TRANSGENIC FOR PRODUCING GENE
TRANSFERRED DENDRITIC CELL CELLS

Kindly insert the following heading and paragraph at page 1, line 4 of the English language specification.

Cross-Reference to Related Applications

This application is the U.S. National Stage of International Application No. PCT/JP2004/016089, filed October 29, 2004, which, in turn, claims the benefit of Japanese Patent Application Nos. 2004-187028, filed June 24, 2004, and 2003-374808, filed November 4, 2003.

Kindly amend the paragraph starting at page 10, line 16 of English language specification as follows.

In addition, the dendritic cells of the present invention include both mature and immature dendritic cells. The immature dendritic cells refer to dendritic cells having low T cell activating ability. Specifically, the immature dendritic cells may have an antigen-presenting ability that is lower than 1/2, preferably lower than 1/4 of that of dendritic cells which maturation had been induced by adding LPS (1 µg/ml) and culturing for two days.

The antigen-presenting ability can be assayed, for example, by allo T cell-activating ability (e.g., a mixed lymphocyte test: allo T cells and dendritic cells are cultured in a mixed culture with a T cell:dendritic cell ratio of 1:10, or preferably with varied ratios; ^3H -thymidine is added 8 hours before terminating cultivation, and the T cell growth capacity is assayed based on the amount of ^3H -thymidine incorporated into the DNA of the T cells. See Fig. 21; Gene Therapy 2000; 7; 249-254) or by the ability to induce specific cytotoxic T cells (CTLs) using a peptide (e.g., a known class I-restricted peptide of a certain antigen is added to dendritic cells; the dendritic cells are co-cultured with T cells obtained from peripheral blood of the same healthy donor from whom the dendritic cells had been obtained (with 25 U/ml or preferably 100 U/ml of IL-2 on day 3 or later) (preferably stimulated three times during 21 days, more preferably twice during 14 days by dendritic cells); the resulting effector cells are co-cultured with ^{51}Cr -labeled target cells (peptide class I-restricted class-I peptide positive tumor cells) at a ratio of 20:1, 10:1, 5:1, or 2.5:1, preferably 100:1, 50:1, 25:1, or 12.5:1, for four hours; and ^{51}Cr released from the target cells is quantified. See Fig. 22; Arch Dermatol Res 292:325-332 (2000)).

Furthermore, the immature dendritic cells preferably have phagocytic ability for antigens, and more preferably show low (for example, significantly low as compared to mature DCs induced by LPS as described above) or negative expression of receptors that induce the costimulation for T cell activation. On the other hand, the mature dendritic cells refer to dendritic cells that have strong antigen-presenting ability for T cell activation or the

like. Specifically, the mature dendritic cells may have an antigen-presenting ability that is half or stronger, preferably equivalent to or stronger than the antigen-presenting ability of dendritic cells in which maturation has been induced by adding LPS (1 µg/ml) and culturing for two days. Furthermore, the mature dendritic cells preferably have weak or no phagocytic ability for antigen, and more preferably show high expression of receptors that induce the costimulation for T cell activation. The activation of dendritic cells refers to the transition from immature to mature dendritic cell; and the activated dendritic cells encompass mature dendritic cells and dendritic cells in the process of the transition, wherein the expression of CD80 and CD86 that induce costimulatory signals are elevated upon the activating stimuli. In CD11c positive dendritic cells, CD83 positivity serves as an indicator of mature dendritic cells.

Kindly amend the paragraph starting at page 12, line 26 of the English language specification as follows.

CD40 is a type I integral membrane protein of 45 to 48 kD (type I integral membrane glycoprotein). ~~Anti-CD40 antibody~~ CD40 is frequently used as a cell marker (Schlossman, S. *et al.*, eds., 1995, Leucocyte Typing V: White Cell Differentiation Antigens. Oxford University Press, New York; Galy, A.H.M.; and H. Spits, 1992, J. Immunol. 149: 775; Clark, E.A. and J.A. Ledbetter, 1986, Proc. Natl. Acad. Sci. 83:

4494; Itoh, H. *et al.*, 1991, Cell 66: 233; Barclay, N.A. *et al.*, 1993, The Leucocyte Antigen Facts Book., Academic Press).

Kindly amend the paragraph starting at page 17, line 31 of the English language specification as follows.

Herein, a minus-strand RNA virus refers to viruses that include a minus strand (an antisense strand corresponding to a sense strand encoding viral proteins) RNA as the genome. The minus-strand RNA is also referred to as negative strand RNA. The minus-strand RNA virus used in the present invention particularly includes single-stranded minus-strand RNA viruses (also referred to as non-segmented minus-strand RNA viruses). The “single-strand negative strand RNA virus” refers to viruses having a single-stranded negative strand [*i.e.*, a minus strand] RNA as the genome. The minus-strand RNA virus includes ~~Such viruses include~~ viruses belonging to Paramyxoviridae (including the genera *Paramyxovirus*, *Morbillivirus*, *Rubulavirus*, and *Pneumovirus*), Rhabdoviridae (including the genera *Vesiculovirus*, *Lyssavirus*, and *Ephemerovirus*), Filoviridae, Orthomyxoviridae, (including Influenza viruses A, B, and C, and Thogoto-like viruses), Bunyaviridae (including the genera *Bunyavirus*, *Hantavirus*, *Nairovirus*, and *Phlebovirus*), Arenaviridae, and the like.

Kindly amend the paragraph starting at page 33, line 26 of the English language specification as follows.

There is no limitation on the foreign gene to be introduced using the minus-strand RNA virus, and naturally occurring proteins include, for example, hormones, cytokines, growth factors, receptors, intracellular signaling molecules, enzymes, and peptides. The proteins may be secretory proteins, membrane proteins, cytoplasmic proteins, nuclear proteins, and the like. Artificial proteins include, for example, fusion proteins such as chimeric toxin, dominant negative proteins (including soluble receptor molecules or membrane bound dominant negative receptors), truncated cell adhesion molecules, and cell surface molecules. The proteins may also be proteins to which a secretory signal, membrane-localization signal, nuclear translocation signal, or the like has been attached. Functions of a particular gene can be suppressed by introducing and expressing antisense RNA molecule, RNA-cleaving ribozyme, or the like as the transfer gene. When a viral vector is prepared using a gene for treating diseases as the foreign gene, gene therapy can be performed through the introduction of the vector. The viral vector of the present invention is applicable to gene therapy wherein the genes are expressed by direct administration or by *ex vivo* administration, and enables expression of foreign genes for which therapeutic effect can be expected, internal genes short in *in vivo* supply, or the like from dendritic cells. In addition, the ~~method~~ vector of the present invention can also be used as a gene therapy vector in regeneration medicine.

Kindly amend the paragraph starting at page 35, line 36 of the English language specification as follows.

Antigens derived from pathogens include, for example, proteins of hepatitis A virus, hepatitis B virus, hepatitis C virus, hepatitis delta virus, papilloma virus antigen, herpes simplex virus (HSV), varicella-zoster virus (VZV), Epstein-Barr virus, Cytomegalovirus (CMV), HIV, malaria, and the like, or partial peptides thereof. The minus-strand RNA viruses encoding such antigen proteins can be used prophylactically or therapeutically. Specifically, envelopes of influenza highly-virulent strain H5N1 for influenza, envelope proteins of Japanese encephalitis virus (Vaccine, vol. 17, No. 15-16, 1869-1882 (1999)) for Japanese encephalitis, HIV and SIV gag proteins (J. Immunology (2000) vol. 164, 4968-4978), HIV envelope proteins, Nef protein, and other viral proteins for AIDS can be mentioned. In addition, for example, cholera toxin B subunit (CTB) (Arakawa T, *et al.*, Nature Biotechnology (1998) 16(10): 934-8, Arakawa T, *et al.*, Nature Biotechnology (1998) 16(3): 292-7) for cholera; rabies virus glycoprotein (Lodmell DL *et al.*, 1998, Nature Medicine 4(8):949-52) for rabies; and capsid protein L1 of human papilloma virus type 6 (J. Med. Virol, 60, 200-204 (2000)) for cervical carcinoma can be mentioned. Antigen proteins of other pathogenic viruses can also be expressed from the vector. Furthermore, it is possible to use JE-E antigen protein of Japanese encephalitis virus (Japanese Patent Application Kokai Publication No. (JP-A) S64-74982

(unexamined, published Japanese patent application), JP-A H1-285498), gD2 protein of human herpes simplex virus (JP-A H5-252965), polypeptides derived from hepatitis C virus (JP-A H5-192160), polypeptides derived from pseudorabies virus (Japanese Patent Kohyo Publication No. (JP-A) H7-502173 (unexamined Japanese national phase publication corresponding to a non-Japanese international publication), and the like. For example, cells derived from patients infected with such pathogenic microorganisms may be analyzed to identify an epitope of an antigen protein to be presented on antigen-presenting cells (APC) for use. It is preferred to appropriately select the HLA type and identify an epitope corresponding to the desired HLA for use.

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REMARKS

The title has been amended and a paragraph cross-referencing related applications has been added. The paragraph starting at page 10, line 16 of English language specification has been amended to recite “class I-restricted peptide.” Support for this change may be found, for example, at page 10, lines 26-27, and is further apparent from the context. The paragraph starting at page 12, line 26, has been amended to recite “CD40 is frequently used as a cell marker.” Support for this change may be found, for example, at page 12, line 26, which recites “CD40.” The paragraph starting at page 17, line 31 has been amended to recite “The minus-strand RNA virus includes.” Support for this change may be found, for example, at page 17, line 31 which recites “a minus-strand RNA virus.” Further support for this change may be found at page 18, lines 1-6, as the exemplified viruses are collectively known in the art as “minus strand RNA viruses.” The paragraph starting at page 33, line 26 has been amended to recite “the vector of the present invention.” Support for this change may be found, for example, at page 34, lines 1-2, which recite “The viral vector of the present invention.” It is further apparent from the context that a vector, rather than a method, (page 34, lines 5-6; emphasis added) “can also be used as a gene therapy vector.” Finally, the paragraph starting at page 35, line 36 has been amended to recite “Japanese encephalitis virus.” Support for this change may be found at page 36, lines 5-6, which recites “Japanese encephalitis virus.” Further, it is

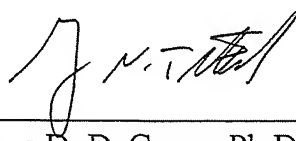
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apparent from the context that the JE-E antigen protein would be of Japanese encephalitis virus, rather than of Japanese encephalitis. These amendments add no new matter.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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